

Application No. 09/965,703  
Amendment dated December 9, 2004  
Reply to Office Action of September 9, 2004

**Amendments to Claims:**

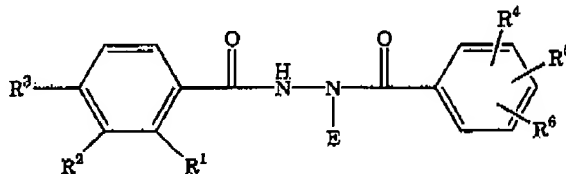
This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

**Claim 1 (cancelled)**

**Claim 2 (cancelled)**

**Claim 3 (previously presented)** A method to modulate the expression of one or more exogenous genes in a subject, wherein the subject is other than a plant, comprising administering to the subject an effective amount of a ligand of the formula:



wherein:

E is a (C<sub>4</sub>-C<sub>6</sub>)alkyl containing a tertiary carbon or a cyano(C<sub>3</sub>-C<sub>6</sub>)alkyl containing a tertiary carbon;

R<sup>1</sup> is H, Me, Et, i-Pr, F, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, SCN, or SCHF<sub>2</sub>;

R<sup>2</sup> is H, Me, Et, n-Pr, i-Pr, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe<sub>2</sub>, NEt<sub>2</sub>, SMe, SEt, SOCF<sub>3</sub>, OCF<sub>2</sub>CF<sub>2</sub>H, COEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, OCF<sub>3</sub>, OCHF<sub>2</sub>, O-i-Pr, SCN, SCHF<sub>2</sub>, SOMe, NH-CN, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R<sup>3</sup> is H, Et, or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

Application No. 09/965,703

Amendment dated December 9, 2004

Reply to Office Action of September 9, 2004

R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently H, Me, Et, F, Cl, Br, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

- a) when R<sup>1</sup> is Me and R<sup>2</sup> is OMe;  
then R<sup>3</sup> is H; and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R<sup>1</sup> is Me and R<sup>2</sup> is OEt;  
then R<sup>3</sup> is H and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;
- c) when R<sup>1</sup> is Et and R<sup>2</sup> is OMe or OEt;  
then R<sup>3</sup> is H and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is:
  - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
  - ii) R<sup>6</sup> is H, R<sup>4</sup> is Me, and R<sup>5</sup> is Et, F, Cl, Br, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R<sup>1</sup> is i-Pr;  
then R<sup>2</sup> is OMe, or OEt; R<sup>3</sup> is H; and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- e) when R<sup>3</sup> is Et;  
then R<sup>2</sup> is H, R<sup>1</sup> is F or Cl, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- f) when R<sup>2</sup> and R<sup>3</sup>, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;  
then R<sup>1</sup> is Me or Et and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- g) when R<sup>2</sup> and R<sup>3</sup>, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;  
then R<sup>1</sup> is Et and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- h) when R<sup>1</sup> is formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, SCN, or SCHF<sub>2</sub>;  
then R<sup>2</sup> is OMe or OEt, R<sup>3</sup> is H, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me; and

Application No. 09/965,703

Amendment dated December 9, 2004

Reply to Office Action of September 9, 2004

- i) when  $R^2$  is Me, Et, n-Pr, i-Pr, formyl,  $CF_3$ ,  $CHF_2$ ,  $CHCl_2$ ,  $CH_2F$ ,  $CH_2Cl$ ,  $CH_2OH$ ,  $CH_2OMe$ ,  $CH_2CN$ , CN,  $C\equiv CH$ , 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc,  $NMe_2$ ,  $NEt_2$ , SMe, SEt,  $SOCF_3$ ,  $OCF_2CF_2H$ ,  $COEt$ , cyclopropyl,  $CF_2CF_3$ ,  $CH=CHCN$ , allyl, azido,  $OCF_3$ ,  $OCHF_2$ , O-i-Pr, SCN,  $SCHF_2$ ,  $SOMe$ , or  $NH-CN$ ;
- then  $R^1$  is Et,  $R^3$  is H, the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;

wherein the cells of the subject contain:

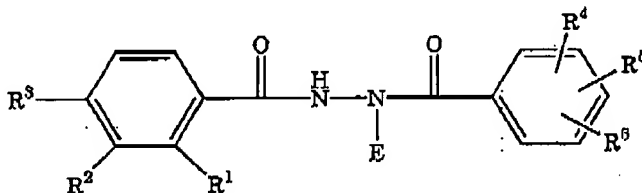
- a) an ecdysone receptor complex comprising:
- 1) a DNA binding domain;
  - 2) a binding domain for the ligand; and
  - 3) a transactivation domain; and
- b) a DNA construct comprising:
- 1) the exogenous gene; and
  - 2) a response element; and

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

**Claim 4 (original):** A method for producing a polypeptide comprising the steps of:

- a) selecting a cell which is substantially insensitive to exposure to a ligand of the formula:



wherein:

E is a  $(C_4-C_6)$ alkyl containing a tertiary carbon or a cyano( $C_3-C_6$ )alkyl containing a tertiary carbon;

$R^1$  is H, Me, Et, i-Pr, F, formyl,  $CF_3$ ,  $CHF_2$ ,  $CHCl_2$ ,  $CH_2F$ ,  $CH_2Cl$ ,  $CH_2OH$ ,  $CH_2OMe$ ,  $CH_2CN$ , CN,  $C\equiv CH$ , 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl,  $CF_2CF_3$ ,  $CH=CHCN$ , allyl, azido, SCN, or  $SCHF_2$ ;

Application No. 09/965,703

Amendment dated December 9, 2004

Reply to Office Action of September 9, 2004

R<sup>2</sup> is H, Me, Et, n-Pr, i-Pr, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C=CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe<sub>2</sub>, NEt<sub>2</sub>, SMe, SEt, SOCF<sub>3</sub>, OCF<sub>2</sub>CF<sub>2</sub>H, COEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, OCF<sub>3</sub>, OCHF<sub>2</sub>, O-i-Pr, SCN, SCHF<sub>2</sub>, SOMe, NH-CN, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R<sup>3</sup> is H, Et, or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently H, Me, Et, F, Cl, Br, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CN, CCH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

- a) when R<sup>1</sup> is Me and R<sup>2</sup> is OMe;  
then R<sup>3</sup> is H; and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R<sup>1</sup> is Me and R<sup>2</sup> is OEt;  
then R<sup>3</sup> is H and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;
- c) when R<sup>1</sup> is Et and R<sup>2</sup> is OMe or OEt;  
then R<sup>3</sup> is H and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is:
  - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
  - ii) R<sup>6</sup> is H, R<sup>4</sup> is Me, and R<sup>5</sup> is Et, F, Cl, Br, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CN, C=CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R<sup>1</sup> is i-Pr;  
then R<sup>2</sup> is OMe, or OEt; R<sup>3</sup> is H; and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- e) when R<sup>3</sup> is Et;

Application No. 09/965,703

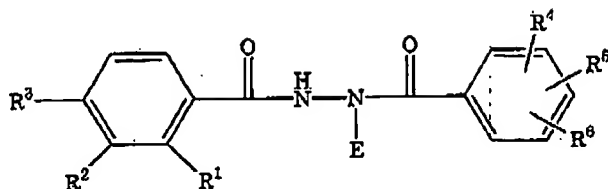
Amendment dated December 9, 2004

Reply to Office Action of September 9, 2004

- then R<sup>2</sup> is H, R<sup>1</sup> is F or Cl, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- f) when R<sup>2</sup> and R<sup>3</sup>, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;  
then R<sup>1</sup> is Me or Et and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- g) when R<sup>2</sup> and R<sup>3</sup>, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;  
then R<sup>1</sup> is Et and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- h) when R<sup>1</sup> is formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, SCN, or SCHF<sub>2</sub>;  
then R<sup>2</sup> is OMe or OEt, R<sup>3</sup> is H, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me; and
- i) when R<sup>2</sup> is Me, Et, n-Pr, i-Pr, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe<sub>2</sub>, NEt<sub>2</sub>, SMe, SEt, SOCF<sub>3</sub>, OCF<sub>2</sub>CF<sub>2</sub>H, COEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, OCF<sub>3</sub>, OCHF<sub>2</sub>, O-i-Pr, SCN, SCHF<sub>2</sub>, SOMe, or NH-CN;  
then R<sup>1</sup> is Et, R<sup>3</sup> is H, the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me;
- b) introducing into the cell:
- 1) a DNA construct comprising:
    - a) an exogenous gene encoding the polypeptide; and
    - b) a response element;wherein the gene is under the control of the response element; and
  - 2) an ecdysone receptor complex comprising:
    - a) a DNA binding domain;
    - b) a binding domain for the ligand; and
    - c) a transactivation domain; and
- c) exposing the cell to the ligand.

**Claim 5 (previously presented)** A method for regulating endogenous or heterologous gene expression in a transgenic organism, wherein the organism is other than plant, comprising contacting a ligand of the formula:

Application No. 09/965,703  
 Amendment dated December 9, 2004  
 Reply to Office Action of September 9, 2004



wherein:

E is a (C<sub>4</sub>-C<sub>6</sub>)alkyl containing a tertiary carbon or a cyano(C<sub>3</sub>-C<sub>5</sub>)alkyl containing a tertiary carbon;

R<sup>1</sup> is H, Me, Et, i-Pr, F, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, SCN, or SCHF<sub>2</sub>;

R<sup>2</sup> is H, Me, Et, n-Pr, i-Pr, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CH<sub>2</sub>OMe, CH<sub>2</sub>CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe<sub>2</sub>, NEt<sub>2</sub>, SMe, SEt, SOCF<sub>3</sub>, OCF<sub>2</sub>CF<sub>2</sub>H, COEt, cyclopropyl, CF<sub>2</sub>CF<sub>3</sub>, CH=CHCN, allyl, azido, OCF<sub>3</sub>, OCHF<sub>2</sub>, O-i-Pr, SCN, SCHF<sub>2</sub>, SOMe, NH-CN, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R<sup>3</sup> is H, Et, or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently H, Me, Et, F, Cl, Br, formyl, CF<sub>3</sub>, CHF<sub>2</sub>, CHCl<sub>2</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, CH<sub>2</sub>OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

- a) when R<sup>1</sup> is Me and R<sup>2</sup> is OMe;  
 then R<sup>3</sup> is H; and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R<sup>1</sup> is Me and R<sup>2</sup> is OEt;  
 then R<sup>3</sup> is H and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;

Application No. 09/965,703

Amendment dated December 9, 2004

Reply to Office Action of September 9, 2004

- c) when  $R^1$  is Et and  $R^2$  is OMe or OEt;  
then  $R^3$  is H and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is:  
i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or  
ii)  $R^6$  is H,  $R^4$  is Me, and  $R^5$  is Et, F, Cl, Br, formyl,  $CF_3$ ,  $CHF_2$ ,  $CHCl_2$ ,  $CH_2F$ ,  $CH_2Cl$ ,  $CH_2OH$ , CN,  $C\equiv CH$ , 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when  $R^1$  is i-Pr;  
then  $R^2$  is OMe, or OEt;  $R^3$  is H; and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;
- e) when  $R^3$  is Et;  
then  $R^2$  is H,  $R^1$  is F or Cl, and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;
- f) when  $R^2$  and  $R^3$ , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;  
then  $R^1$  is Me or Et and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;
- g) when  $R^2$  and  $R^3$ , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;  
then  $R^1$  is Et and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;
- h) when  $R^1$  is formyl,  $CF_3$ ,  $CHF_2$ ,  $CHCl_2$ ,  $CH_2F$ ,  $CH_2Cl$ ,  $CH_2OH$ ,  $CH_2OMe$ ,  $CH_2CN$ , CN,  $C\equiv CH$ , 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl,  $CF_2CF_3$ ,  $CH=CHCN$ , allyl, azido, SCN, or  $SCHF_2$ ;  
then  $R^2$  is OMe or OEt,  $R^3$  is H, and the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me; and
- i) when  $R^2$  is Me, Et, n-Pr, i-Pr, formyl,  $CF_3$ ,  $CHF_2$ ,  $CHCl_2$ ,  $CH_2F$ ,  $CH_2Cl$ ,  $CH_2OH$ ,  $CH_2OMe$ ,  $CH_2CN$ , CN,  $C\equiv CH$ , 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe<sub>2</sub>, NEt<sub>2</sub>, SMe, SEt,  $SOCF_3$ ,  $OCF_2CF_2H$ , COEt, cyclopropyl,  $CF_2CF_3$ ,  $CH=CHCN$ , allyl, azido,  $OCF_3$ ,  $OCHF_2$ , O-i-Pr, SCN,  $SCHF_2$ , SOMe, or NH-CN;  
then  $R^1$  is Et,  $R^3$  is H, the combination  $R^4$ ,  $R^5$ , and  $R^6$  is 3,5-di-Me;

with an ecdysone receptor complex within the cells of the organism wherein the cells further contain a DNA binding sequence for the ecdysone receptor complex when in combination with the ligand and wherein formation of an ecdysone receptor complex-ligand-DNA binding sequence complex induces expression of the gene.

Application No. 09/965,703  
Amendment dated December 9, 2004  
Reply to Office Action of September 9, 2004

**Claim 6 (cancelled)**

**Claim 7 (original)** The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl; R<sup>1</sup> is Me, Et, i-Pr, or F; R<sup>2</sup> is OH, OMe, OEt, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R<sup>3</sup> is H, Et or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently Me, F, Cl, CH<sub>2</sub>OH, or OMe.

**Claim 8 (original)** The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl; R<sup>1</sup> is Me, Et, i-Pr, or F; R<sup>2</sup> is OH, OMe, OEt, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R<sup>3</sup> is H, Et or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently Me, F, Cl, CH<sub>2</sub>OH, or OMe.

**Claim 9 (original)** The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl; R<sup>1</sup> is Me, Et, i-Pr, or F; R<sup>2</sup> is OH, OMe, OEt, or joined with R<sup>3</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R<sup>3</sup> is H, Et or joined with R<sup>2</sup> and the phenyl carbons to which R<sup>2</sup> and R<sup>3</sup> are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are independently Me, F, Cl, CH<sub>2</sub>OH, or OMe.

**Claim 10 (cancelled)**

**Claim 11 (original)** The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl, R<sup>1</sup> is Et, R<sup>2</sup> is OEt, R<sup>3</sup> is H, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me.

**Claim 12 (original)** The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl, R<sup>1</sup> is Et, R<sup>2</sup> is OEt, R<sup>3</sup> is H, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me.

**Claim 13 (original)** The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl, R<sup>1</sup> is Et, R<sup>2</sup> is OEt, R<sup>3</sup> is H, and the combination R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is 3,5-di-Me.



Application No. 09/965,703  
Amendment dated December 9, 2004  
Reply to Office Action of September 9, 2004

**Claim 14 (cancelled)**

**Claim 15 (original)** The method of Claim 3 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

**Claim 16 (original)** The method of Claim 4 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

**Claim 17 (original)** The method of Claim 5 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

**Claim 19 (original)** The method of Claim 3 wherein the subject is a mammal.

**Claim 20 (previously presented)** The method of Claim 3 wherein the subject is a fungus or yeast.

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